

What is Claimed is:

1. A method for diagnosing a medically relevant condition of a patient, comprising the steps of:
 - 5 (a) obtaining a raw sample containing cells or cell debris from a patient;
 - (b) preparing a sample solution from the raw sample;
 - (c) detecting the levels of one or more relevant markers characteristic for said medically relevant condition in said sample solution;
 - (d) detecting the levels of one or more normalization markers characteristic for at least 10 one of the following normalization parameters:
 - the presence or absence of a particular cell type among the cells represented within the sample solution,
 - the presence or absence of a particular differentiation pattern in the cells represented within the sample solution,
 - 15 the presence or absence of particular proliferation properties of the cells represented within the sample solution,
 - (e) normalizing the detected levels of said one or more relevant markers with respect to said at least one of the normalization parameters; and
 - (f) diagnosing the medically relevant condition based on the normalized levels of the 20 relevant markers to the normalization parameters.
2. The method according to Claim 1, wherein the medically relevant condition is a condition characterized by a property selected from the group consisting of the presence or absence of particular cell types in a sample, the presence or absence of a particular 25 differentiation pattern related to cells within the sample, and the presence or absence of proliferative characteristics of cells within the sample.

3. The method according to Claim 2, wherein the medically relevant condition is a disease.
4. The method according to Claim 3, wherein the disease is a cell proliferative disorder, cancer or a precursory lesion.
5. The method according to Claim 4, wherein the cancer is cancer of the head and the neck, cancer of the respiratory tract, cancer of the gastrointestinal tract, cancer of the skin and its appendages, cancer of the central and peripheral nervous system, cancer of the urinary system, cancer of the reproductive system, anogenital cancer, cancer of the endocrine system, cancer of the soft tissues and bone, or cancer of the lymphopoietic and hematopoietic system.
- 10 6. The method according to Claim 1, wherein the raw sample is blood, a secretion, a swab, an aspirate, a lavage, sputum, saliva, stool, bile, a cell, a tissue, a biopsy or a body fluid.
7. The method according to Claim 6, wherein the raw sample contains cells of an eukaryotic or prokaryotic organism.
8. The method according to Claim 1, wherein the one or more relevant markers are selected from the group consisting of cell cycle regulatory proteins, metalloproteinases, transmembrane proteins, calcium binding proteins, growth factors, marker molecules characteristic for viral infections, cell proliferation markers, and markers associated with DNA replication, tumor marker proteins, and the nucleic acids coding for the respective proteins.
- 15 9. The method of Claim 8, wherein the tumor marker proteins are selected from the group consisting of cyclin dependent kinase inhibitors, p53, pRb, p14ARF, cyclin E, cyclin A, cyclin B, MN, her2/neu, mdm-2, bcl-2, EGF-Receptor, MCM2, MCM3, MCM4, MCM5, MCM6, MCM7, CDC2, CDC6, CDC7 protein kinase, CDC14 protein phosphatase, Dbf4, PCNA, Ki67, KiS1, Id1, osteopontine, GRP, renal dipeptidase, and TGF β II receptor.
- 20 10. The method according to Claim 9, wherein the cyclin-dependent kinase inhibitor is selected from the group consisting of p16^{INK4a}, p13.5, p14, p15, p19, p21, p27.

11. The method according to Claim 8, wherein the marker molecules characteristic for viral infections are a viral protein or a viral nucleic acid.

12. The method according to Claim 11, wherein the viral protein or the viral nucleic acid is a HPV protein or a nucleic acid derived from a HPV gene selected from the group consisting of
5 HPV L1, HPV L2, HPV E1, HPV E2, HPV E4, HPV E5, HPV E6 and HPV E7.

13. The method according to Claim 1, wherein the one or more normalization markers are selected from the group consisting of cell surface proteins, housekeeping genes, receptor proteins, glycoproteins and/or proteoglycans, carbohydrate structures specific for glycoproteins and/or proteoglycans, cell cycle regulatory proteins, metalloproteinases, transmembrane
10 proteins, calcium binding proteins, growth factors, cell differentiation markers, and proteins associated with DNA replication.

14. The method according to Claim 13, wherein the one or more normalization markers are an epithelial antigen, a cytokeratin or a CD antigen.

15. The method according to Claim 13, wherein the one or more normalization markers are selected from the group consisting of a glycoprotein, a proteoglycan, and a carbohydrate structure present on these molecules.
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16. The method according to Claim 13, wherein the one or more normalization markers are an enzyme involved in the biosynthesis of glycoproteins and/or proteoglycans.

17. The method of Claim 1, wherein the detection of the relevant markers or the
20 normalization markers is performed using at least one probe specifically recognizing and binding to said marker molecules.

18. The method according to Claim 17, wherein at least one probe is detectably labelled.

19. The method according to Claim 18, wherein the probe is labelled by a radioisotope, a
bioluminescent compound, a chemiluminescent compound, an electroluminescent compound, a
25 fluorescent compound, a metal chelate, an enzyme, or a biologically relevant binding structure.

20. The method according to Claim 19, wherein the biologically relevant binding structure is biotin, avidin, streptavidin or digoxigenin.

21. The method according to Claim 17, wherein said at least one probe is a binding agent.

22. The method according to Claim 21, wherein said binding agent specifically binds to a 5 marker polypeptide.

23. The method according to Claim 21, wherein the binding agent is an antibody, an antibody fragment, a miniantibody, or a peptidomimetic comprising an antigen binding epitope.

24. The method according to Claim 17, wherein said at least one probe is a lectin comprising a carbohydrate binding site, or a carbohydrate specifically recognized by a lectin.

10 25. The method according to Claim 17, wherein said at least one probe is a nucleic acid molecule complementary or reverse-complementary to a marker nucleic acid and wherein said probe is specifically hybridizing to said marker nucleic acid.

26. The method according to Claim 25, wherein the detection comprises a quantitative or 15 semi-quantitative amplification reaction.

27. A test kit for diagnosing a medically relevant condition comprising:

(a) at least one reagent for the detection of at least one marker molecule characteristic for a medically relevant condition; and

20 (b) at least one reagent for the detection of at least one normalization marker characteristic for at least one of the following parameters:

the presence or absence of a particular cell type or differentiation, pattern in the cells represented within the sample solution, and the presence or absence of particular proliferation properties of the cells represented 25 within the sample solution; and

(c) a buffer for solubilizing samples.

28. The test kit according to Claim 27, wherein at least one reagent is fixed to a solid phase.

29. The test kit according to Claim 27, furthermore comprising at least one of the following components:

5 (a) at least one marker molecule for carrying out positive control reactions selected from the group consisting of:

(i) relevant marker molecules characteristic for medically relevant conditions,

(ii) normalization marker molecules characteristic for at least one of the following parameters:

10 (1) the presence or absence of a particular differentiation pattern in the cells represented within the sample solution

(2) the presence or absence of particular proliferation properties of the cells represented within the sample solution; and

(b) reagents and buffers commonly used for carrying out the detection reaction.

15 30. The test kit according to Claim 27, wherein the reagents for detection of marker molecules comprise binding agents specific for said marker molecules and/or nucleic acid probes hybridizing to nucleic acids coding for said marker molecules.

20 31. The test kit according to Claim 30, wherein the binding agents are an antibody, a miniantibody, or a peptidomimetic comprising an antigen binding epitope.

32. The test kit according to Claim 27, wherein the test kit is a diagnostic test kit, a research kit, or an analytical kit.

25 33. A method for diagnosing cervical dysplasia, cervical cancer and their respective precursor stages in human cervical body samples comprising:

preparing a sample solution from a human cervical sample;

- detecting the level of at least one relevant marker characteristic for the presence of cervical dysplasia;
- detecting the level of at least one normalization marker characteristic for the presence of epithelial cells;
- 5 normalizing the levels of the relevant markers to the levels of the normalization markers detected within the sample solution; and
- diagnosing cervical dysplasia based on the normalized levels of the relevant markers to the normalization markers.

34. The method according to Claim 33, wherein said at least one relevant marker
10 characteristic for the presence of cervical dysplasia is selected from the group consisting of
p16^{INK4a}, an HPV associated marker, p14ARF, p19, p21, p27, pRb, p53, cyclin E, cyclin A,
cyclin B, MN, her2/neu, mdm-2, bcl-2, EGF-Receptor, MCM2, MCM3, MCM4, MCM5,
MCM6, MCM7, CDC2, CDC6, CDC7 protein kinase, CDC14 protein phosphatase, Dbf4,
PCNA, Ki67, KiS1, Id1, osteopontine, claudin-1, GRP, renal dipeptidase, and TGF β II receptor.

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35. The method according to Claim 33, wherein said at least one normalization marker
characteristic for the presence of epithelial cells is selected from the group consisting of
gamma-Catenin, Ep-Cam, E-Cadherin, alpha-Catenin, beta-Catenin, Desmoplakin, hKLK13,
SCCA, uPA1, Involucrin, CK8, CK18, CK10, CDK13, vimentin, concanavalin A receptor, and
20 lectins.

36. The method according to Claim 33, wherein said method is used in early detection or
primary screening tests of cervical lesions.

25 37. The method according to Claim 33, wherein said human cervical body sample is a
swab, a secretion, an aspirate, a lavage, a cell, a tissue, a biopsy or a body fluid.

38. The method according to Claim 33, wherein said epithelial cells are ectocervical or
endocervical cells.

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39. The method according to Claim 38, wherein a normalization marker indicating the presence of endocervical cells is selected from the group consisting of Ep-Cam, CK8, or CK18.

40. The method according to Claim 38, wherein a normalization marker indicating the presence of endocervical cells is selected from the group consisting of gamma-Catenin, E-Cadherin, alpha-Catenin, beta-Catenin, CK13, p120, or Involucrin.

41. A test kit for diagnosing cervical dysplasia comprising:

(a) at least one reagent for the detection of at least one marker molecule characteristic for cervical dysplasias selected from the group consisting of p16^{INK4a}, p14ARF, cyclin E, cyclin A, cyclin B, MN, her2/neu, mdm-2, bcl-2, EGF-Receptor, mcm-2, mcm-5, claudin-1, markers indicative for Human papilloma virus infection, pRb, and p53; and

(b) at least one reagent for the detection of at least one normalization marker characteristic for the presence or absence of epithelial cells selected from the group consisting of CK8, Ep-Cam, CK13, CK8, CK18, E-Cadherin, alpha-Catenin, beta-Catenin, gamma-Catenin, or Involucrin.

42. The test kit according to Claim 41, wherein at least one reagent is fixed to a solid phase.

43. A test kit according to Claim 41, furthermore comprising at least one of the following components:

(a) at least one marker molecule for carrying out positive control reactions selected from the group consisting of:

(i) relevant marker molecules characteristic for cervical dysplasia,

(ii) normalization marker molecules characteristic for at least one of the following parameters:

(1) the presence or absence of columnar epithelial cells;

(2) the presence or absence of squamous epithelial cells; and

(b) reagents and buffers commonly used for carrying out the detection reaction.

44. The test kit according to Claim 41, wherein the reagents for detection of marker molecules comprise binding agents specific for said marker molecules and/or nucleic acid probes hybridizing to nucleic acids coding for said marker molecules.

5 45. The test kit according to Claim 44, wherein the binding agents are an antibody, a miniantibody, or a peptidomimetic comprising an antigen binding epitope.

10 46. The test kit according to Claim 41, wherein the test kit is a diagnostic test kit, an in-vitro diagnostic device, a research kit, or an analytical kit.

47. A test kit comprising:

15 (a) a reagent for the detection of p16^{INK4a}; and

(b) a reagent for the detection of gamma-Catenin.

48. The test kit according to Claim 47 furthermore comprising a reagent for the detection of Ep-Cam.

20 49. The test kit according to Claim 47, further comprising a buffer for sample lysis.

50. The test kit according to Claim 47, wherein the reagents for the detection of p16^{INK4a} and gamma-Catenin are fixed to solid phases.

51. The test kit according to Claim 47, wherein the test kit is an in-vitro diagnostic device.